

Fig. 1a)

1 / 18

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1      gaggaggccc gagaggagtc ggtgggcagcg gcgggcggcgg gaccgggcagc agcagcagca
61     gcagcagcag caaccactag cctcctgccc cgcggcgcttg cgacgagccc caccgagccgc
121    tcaccccgcc gttctcagcg ctgcccgacc ccgctggcgc gcctcccgcc gcagtcccgg
181    cagcgccctca gttgtcctcc gactcgccct cggccttcgc gcagcgcagc acagccgcac
241    gcaccgcagc acagcacagc acagcccagg catagcttcg gcacagcccc ggctccggct
301    cctgcggcag ctccctctggc acgtccctgc gccgacattc tggagggttg atgctcttgt
361    ccaaaatcaa ctcgcttgcc cactcgcgcg ccgcgccttg caacgacctg caccgaccca
421    agctggcgcc cggcaaggag aaggagcccc tggagtcgca gtaccagggt ggcccgctac
481    tgggcagcgg cggcttcggc tcggctctact caggcatccg cgtctccgac aacttgccgg
541    tggccatcaa acacgtggag aaggaccgga tttccgactg gggagagctg cctaattggca
601    ctcgagtgcc catggaagtg gtccctgctga agaagggtgag ctcggttttc tccggcgctca
661    ttaggctcct ggactgggtc gagaggcccc acagtttctg cctgatccct gagaggcccc
721    agccggtgca agatctcttc gacttcatca cggaaagggg agccctgcaa gaggagctgg
781    cccgcagctt cttctggcag gtgctggagg ccgtgcggca ctgccacaac tgcggggtgc
841    tacaccgcga catcaaggac gaaaacatcc ttatcgacct caatcgcggc gagctcaagc
901    tcatcgactt cgggtcgggg gcgctgctca aggacaccgt ctacacggac ttcgatggga
961    cccgagtgtg tagccctcca gagtggatcc gctaccatcg ctaccatggc aggtcggcgg
1021   cagtctggtc cctggggatc ctgctgtatg atatgggtgtg tggagatatt cctttcgagc
1081   atgacgaaga gatcatcagg ggccagggtt tcttcaggca gaggtctctc tcagaatgtc
1141   agcatctcat tagatgggtg ttggccctga gaccatcaga taggccaacc ttcgaagaaa
1201   tccagaacca tccatggatg caagatgttc tctgccccca ggaaactgct gagatccacc
1261   tccacagcct gtcgcccggg cccagcaaat agcagccttt ctggcaggtc ctccctctc
1321   ttgtcagatg cccgagggag gggaagcttc tgtctccagc tttccgagta ccagtgcac
1381   gtctcgccaa gcaggacagt gcttgatata ggaacaacat ttacaactca ttccagatcc
1441   caggccccct gaggctgcct cccaacagtg gggaagagtg actctccagg ggtcctaggc
1501   ctcaactcct cccatagata ctctcttctt ctcatagggt tccagcattg ctggactctg
1561   aaatatcccc ggggtggggg gtgggggtgg gcagaaccct gccaatggaa ctctttcttc
1621   atcatgagtt ctgctgaatg ccgcgatggg tcaggtaggg gggaaacagg ttgggatggg
1681   ataggactag cacattttaa gtccctgtca cctcttcga ctctttctga gtgccttctg
1741   tggggactcc ggctgtgctg ggagaaatac ttgaacttgc ctcttttacc tgctgcttct
1801   ccaaaaatct gcctgggttt tgttccctat ttttctctcc tgtcctccct caccctctcc
1861   ttcatatgaa aggtgccatg gaagaggcta caggggccaaa cgctgagcca cctgcccttt
1921   tttctgcctc ctttagtaaa actccgagtg aactggtctt cctttttggg ttttacttaa
1981   ctgtttcaaa gccaagacct cacacacaca aaaaaatgca caaaccaagc aatcaacaga
2041   aaagctgtaa atgtgtgtac agttggcatg gtagtatata aaaagattgt agtggatcta
2101   atttttaaga aattttgcct ttaagttatt ttacctgttt ttgtttcttg ttttgaaaga
2161   tgcgcattct aacctggagg tcaatgttat gtatttattt atttatttat ttggttcctt
2221   tcctattcca agcttccata gctgctgccc tagttttctt tctccttttc ctctctgac
2281   ttggggacct tttgggggag ggctgcgacg cttgctctgt ttgtggggtg acgggactca
2341   ggcgggacag tgctgcagct ccctggcttc tgtggggccc ctcacctact taccaggtg
2401   ggtcccggct ctgtgggtga tgggaggggc cattgctgac tgtgtatata ggataattat
2461   gaaacacagt tctggatggt gtgccttcca gatcctctct ggggctgtgt tttgagcagc
2521   aggtagcctg ctggttttat ctgagtgaaa tactgtacag ggaataaaaa gagatcttat
2581   ttttttttta tacttgcggt tgggaataaaa accctttggc ttt

```

Fig. 1b)

```
1      mllskinsla hlraapcndl hatklapgke keplesqyqv gpllsgggfg svysgirvsd
61     nlpvaikhve kdrisdwgel pngtrvpmev vllkkvssgf sgvirlldwf erpdsfvlil
121    erpepvqdlf dfitergalq eelarsffwq vleavrhchn cgvlhrdikd enilidlnrg
181    elklidfgsg allkdtvytd fdgtrvyspp ewiryhryhg rsaavwslgi llydmvcgdi
241    pfehdeeir  gqvffrqrvs secqhlirwc lalrpsdrpt feeiqnhpwm qdvllpqeta
301    eihlhslspg psk
```

Fig. 1c)

3 / 18

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1      gggatgctct tgtccaagat caactccctg gcccacctgc gcgcagcccc ttgcaacgac
61     ctgcacgcca acaagctggc gccgggcaaa gagaaggagc ccctggagtc gcagtaccag
121    gtgggccccg tgttgggcag cggtggtctt ggctcggctt actcgggcat ccgcgtcgcc
181    gacaacttgc cggtgggccat caagcacgtg gagaaggacc ggatttccga ctggggggaa
241    ctgcccacg gcacccgagt gcccatggaa gtggtcctgc tgaagaaggt gagctcgggc
301    ttctcgggcg tcattagact tctggactgg ttcgagaggc ccgatatgtt cgtgctgac
361    ctggagaggc ccgaaccogt gcaagacctc ttcgacttca tcaccgagcg aggagccctc
421    caggaggagc tggcccggag cttcttcttg cagggtgctg aggccgtgcg gcattgccac
481    aactgcgggg ttctccaccg cgacatcaag gacgagaaca tcttaatcga cctgaaccgc
541    ggcgaactca aactcatcga cttcgggtcg ggggcgctgc tcaaggacac agtctacacg
601    gactttgacg gaaccgagt gtacagtcct ccagagtgga ttcgctacca tcgctaccac
661    ggcaggtcgg ctgctgtttg gtccctgggg atcctgctct atgacatggt ctgcgagat
721    attccatttg agcacgacga agagatcgtc aaggggccaag tgtactttag gcaaagggtc
781    tcttcagaat gtcaacatct tattagatgg tgctgtccc tgagaccatc ggaccggccc
841    tcctttgaag aaatccagaa ccatccgtgg atgcaggatg ttctcctgcc ccaggccacc
901    gccgagattc atctgcacag cctgtcacca tcaccagca aatagcagcc attctgtcag
961    accctccagg gaagagagag cttgtctgct ggccctccaac aggaccctgc tctacgatgc
1021   agggacagaa atgacaactc attccaggct ccgggggtccc tggagcaacc tcctcaagg
1081   agaagagact agttcactcg tcctggaccc cgctttgccc ctcacagact cagtggcgtc
1141   cagtgtggct ggcgtccgca gagtcccggg tgttgggggg ggaggtggga gtgggtcaga
1201   gccctgtcat ggaactttag tcaccatgga gactgtgggt caccaagatg ggccagggtg
1261   ggggaaaaac atttgggggg tgggattaaa aactagcacc at
```

**Fig. 1d)**

4 / 18

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1      mllskinsla hlraapcndl hanklapgke keplesqyqv gp11gsggfg svysgirvad
61     nlpvaikhve kdridswgel pngtrvpmev vllkkvssgf sgvirlldwf erpdsfvlil
121    erpepvqdlf dfitergalq eelarsffwq vleavrhchn cgvlhrdikd enilidlnrg
181    elklidfgsg allkdtvytd fdgtrvyspp ewiryhryhg rsaavwslgi llydmvcgdi
241    pfehdeeivk gqvyfrgrvs secqhlirwc lslrpsdrps feeiqnhpwm qdvllpqata
301    eihlhlslsps psk
```

```
1   atgctcctgt ccaagatcaa ctccctggcc cacctgcgcg cccgcccctg caacgacctg
61  cacgccacca agctggcgcc gggcaaagag aaggagcccc tggagtcgca gtaccaggtg
121 ggcccgtgtg tgggcagcgg tggcttcggc tcggtctact ctggcatccg cgtcgccgac
181 aacttgccgg tggccattaa gcacgtggag aaggaccgga tttccgattg gggagaactg
241 cccaatggca cccgagtgcc catggaagtg gtcctgttga agaaggtag ctcggaactc
301 tcgggcgtca ttagacttct ggactgggtc gagaggcccc atagtctcgt gctgacacctg
361 gagaggcccc aaccggtgca agacctcttc gactttatca ccgaacgagg agccctacag
421 gaggacctgg cccgaggatt cttctggcag gtgctggagg ccgtgcggca ttgccacaac
481 tgcgggggtc tccaccgcga catcaaggac gagaacatct taatcgacct gagccgcggc
541 gaaatcaaac tcatcgactt cgggtcgggg gcgctgctca aggacacagt ctacacggac
601 tttgatggga cccgagtgtg cagtcctcca gagtggattc gctaccatcg ctaccacggc
661 aggtcggcag ctgtctggtc ccttgggata ctgctctatg acatggtctg cggagatatt
721 ccgtttgagc acgatgaaga gatcatcaag ggccaagtgt tcttcaggca aactgtctct
781 tcagagtgtc agcaccttat taaatgggtg ctgtccctga gacggtcaga tcggccctcc
841 tttgaagaaa tccggaacca tccgtggatg cagggtgacc tcctgcccc a ggcagcttct
901 gagatccatc tgcacagtct gtcaccggga tccagcaagt ag
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Fig. 1f)

6 / 18

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1      mllskinsla hlrarpcndl hatklapgke keplesqyqv gp1lgsgggfg svysgirvad
61     nlpvaikhve kdrisdwgel pngtrvpmev vllkkvssdf sgvirllldwf erpdsfvlil
121    erpepvqdlf dfitergalq edlargffwq vleavrhchn cgvlhrdikd enilidlsrg
181    eiklidfgsg allkdtvytd fdgtrvyspp ewiryhryhg rsaavwslgi llydmvcgdi
241    pfehdeeiik gqvffrqtvS secqhlikwc lslrpsdrps feeirnhpwm qgdllpqaas
301    eihlhlslspg ssk
```

Fig. 2a)

7 / 18

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1      cccacgcgtc cgcagagtgc cagcagctga tccggtggtg cctgtccctg cggccctcag
61     agcggccgtc gctggatcag attgcggccc atccctggat gctgggggct gacgggggcg
121    ccccgagagag ctgtgacctg cggctgtgca ccctcgaccc tgatgacgtg gccagcacca
181    cgtccagcag cgagagcttg tgaggagctg cacctgactg ggagctaggg gaccacctgc
241    cttggccaga cctgggacgc ccccagaccc tgactttttc ctgctggtggc cgtctcctcc
301    tgcggaagca gtgacctctg acccttggtg accttcgctt tgagtgcctt ttgaacgctg
361    gtcccgcggg acttggtttt ctcaagctct gtctgtccaa agacgctccg gtcgaggtcc
421    cgccctgccct ggggtggatac ttgaacccca gacgcccctc tgtgctgctg tgtccggagg
481    cggccttccc atctgcctgc ccaccggag ctctttccgc cggcgagggg tccaagccc
541    acctcccgcc ctgagtcctg cgggtgtgct ctgggcacgt cctgcacaca caatgcaagt
601    cctggcctcc gcgcccgcgc gccacgcga gccgtaccg cgcgcaactc tgttatttat
661    ggtgtgacct cctggagggtg cctcggccc accggggcta tttattgttt aatttatttg
721    ttgaggttat ttcctctgag cagtctgcct ctcccaagcc ccaggggaca gtggggaggc
781    aggggagggg gtggtgtgtg tccagggacc ccaggccctg attcctgtgc ctggcgtctg
841    tcctggcccc gcctgtcaga agatgaacat gtatagtggc taacttaagg ggagtgggtg
901    accctgacac ttccaggcac tgtgcccagg gtttgggttt taaattattg actttgtaca
961    gtctgcttgt gggctctgaa agctgggggtg gggccagagc ctgagcgttt aatttattca
1021   gtacctgtgt ttgtgtgaat gcggtgtgtg caggcatcgc agatgggggt tctttcagtt
1081   caaaagtgag atgtctggag atcatatttt tttatacagg tatttcaatt aaaatgtttt
1141   tgtacataaa aaaaaaaaaa aaaaaaaaaa aaaaaa
```

Fig. 2 b)

8 / 18

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1      cgctcggcca gctgccgtct acgggcttcc gcgcggccac cgggcaactg cgccgcgcgg
61     ctgccccact gagcgctcgg cctcggggcc gtgggatccg ccgcgctgtc tgcggtcagg
121    aagaccgccc tcccgcgtcc gtgccggacg ggtcagaggc ggcgccgcac gcgaggccac
181    ccgcgatgct gctgtccaag ttccggctccc tggcgcacct ctgcgggcct ggcggcgtgg
241    accacctccc agtgaagatc ctacagccag ccaaggcgga caaggagagc ttcgagaagg
301    tgtaccaggt gggcgccgtg ctccggcagcg gcggcttcgg cacggtctac gcgggcagcc
361    gcatcgccga cggactcccg gtggctgtga agcacgtggt gaaggagcgg gtgaccgagt
421    ggggcagtcct cggcggaatg gccgtgcccc tggagggtgg gctgctgcgc aagggtggcg
481    cggcgggcgg cgcgcgcggc gtcacccgcc tgctggactg gttcgagcgg cccgacggct
541    tcctgctggt gctggagcga cccgagccgg cacaggacct cttcgacttc atcactgaac
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781    cggctctacac tgactttgat ggcacccgtg tgtacagccc cccagagtgg atccggtatc
841    atcgatatca cgggcggtct gccactgtgt ggtctctggg tgtactgtc tacgacatgg
901    tgtgtgggga cattcccttt gagcaggatg aggagatctt gcgcggcagg ctctttttcc
961    ggaggagggt ctccccagag tgccagcagc ttattgagtg gtgtctctcc ctgcggccct
1021   cagagaggcc ctcgctggac caaattgctg cccatccctg gatgctgggg acagagggca
1081   gcgttccaga gaactgtgac cttcggctct gtgccctgga tactgatgac ggagccagta
1141   ccacttccag cagtgaagagc ttgtgaggag gaggaggggc ctggactcca cactgggggc
1201   ctgggctcag cctagccagc cctctcccag aatgaacatt ttctgcctgg gatgtctcct
1261   gcaaaaagcag tgacctctga cccctggtga cctttgctct cggcacccgg cctgtttcct
1321   ttgcttttag tgcttttttg aacgctgtct cacagggcct gggttttctt gagctcttct
1381   gtccaaagat ggctgcgggc taagcaaggc cccgcctgcc ctgggtggat acttgaaccc
1441   gagaccctac cctgctgtct catcttgagg cagccttcct gaccaagtgt gtttgacatg
1501   gagcgccctg tgggtgccac ctccaacct ccagtctcct ggtcttcgtc tgggcatgtc
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1981   cagagtctca agcccttaat ttatttttag aactgtgttc tgtgacctg gtgtgagtag
2041   gcatcagggg tggggttgta taagttcaaa agtgtgaaat gtctggagat catatttttt
2101   atacaggtat ttcaattaaa tgttttggta tat

```



```
1      mllskfgsla hlcgpggvdh lpvkilqpak adkesfekvy qvgavlgsgg fgtvyagsri
61     adglpvavkh vvkervtewg slggmavple vlllrkvgaa ggargvirll dwferpdgfl
121    lvlerpepaq dlfdfiterg aldeplarrf faqvlaavrh chncgvvhrd ikdenllvdl
181    rsgelklidf gsgavlkdtv ytdfdgtrvy sppewiryhr yhgrsatvws lgvllydmvc
241    gdipfeqdee ilrgrlffrr rvspecqqli ewclslrpse rpsldqiaah pwmlgtegs
301    pencdlrlca ltdddgastt sssesl
```

Fig. 2 d)

```

1      gcagggcggg tgagagcgcc gtgaaagccg cggaacgccc tgcacctccg cgactctact
61     acggcaagct agtccggacg ggtcgtcgtc cccgcgcgcc accagccctt ggtgaaacga
121    cagggagcgt ccggcttccc cagcaccgcc ctgcgagact caaaacagcc acaccgcaaa
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301    ctgccgtcta cgcgcttttc cgcggccacc gggcaactgc gccgcgcggc tgccccgctg
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421    cccgcgtcct tgccggacgg gtcagaggcg gcaccgcacg cgaggccacc cgcgatgctg
481    ctgtccaagt tcggctccct ggcgcacctc tgcgggcctg gcggcgtgga ccacctcca
541    gtgaagatcc tacagccagc caaggetgac aaggagagct tcgagaaggt gtaccaggtg
601    ggcgcctgct tgggcagcgg cggcttcggc acggtctacg cgggcagccg catcgccgac
661    ggactcccgg tggctgtgaa gcacgtggtg aaggagcggg tgaccgagtg gggcagctct
721    ggcggagtg ggcgtgcccc ggaggtggtg ctgctgcgca aggtgggcgc ggcgggcggc
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841    ctggagcgac ccgagccggc acaggacctc ttcgacttca tcaactgaac aggcgccctg
901    gacgagccgc tggcgcgtcg cttcttcgcg caggtgcttg ccgctgtgcg gacactgcc
961    aattgtgggg tcgtgcaccg cgacatcaag gacgagaacc tgctggtgga cctgcgctcg
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1381   aactgtgacc ttcggccttg tgccctggat actgacgacg gagccagtac cacttccagc
1441   agtgagagct tgtgaggagg agaagggggc tgggctcggc ctagccagcg ctctcccaga
1501   attgaacact ttctgcctgg gatgtctgct gcaaaagcag tgacctctga cccctggtga
1561   cctttgctct cggcaccggg cctgtttcct ttgctttgag tgcccttttg aacgctgctc
1621   cacagggcct gggttttctt gagctcttct gtccaaagat ggctgagggc taagcaaggt
1681   cctgccctgg gtggataact gaaccagaga tcccgaacct gctgctccat ctgaggaggc
1741   agccttctctg accaagtgtg tttgacatgg agcgcctctg ggtgcccacc tccaaccctc
1801   cagtctcctg gtgttcatct gggcatgtct gcacaagcaa tgcaacgctg ggccactgct
1861   gcccgctctg ctccccggca cggcacggct ccgcacgcaa cctaagcgtg ccaccacggt
1921   ctcttatttta tgggtgtgat accctggagg gcgcccccg cctgctgggg ctattttattg
1981   tttaatttat ttgctgaggt tcctccaagc aaccaccttc tccaggcccc tggggtgttg
2041   aaagtcaaat gtggctgttg agtccacaga ccccatcct aattcctgca cctggaggag
2101   tcccccaacc cccgtgtttg cgggaggaag catttgtaca gtggctaatt taaggggagt
2161   gggagaccct gtcaccctga gcactctgcg ctggggaggg gtttaaatta ttgacctgt
2221   acagtctgct tgctggctct gaaagctggg gttgggggac agagtctcaa gcccttaatt
2281   tatttttagca gctgtgtttc tgtgacctg gtgtgactaa gcatcagggg tggggttgta
2341   taagttcaaa agtgtgaaat gtctgaagat catatttttt atacagggtat ttcaattaaa
2401   tgttttggtg tataatggaa aaaaaaaaaa aaaaaaaaaa aaaaaaa

```

|     |            |            |            |             |            |            |
|-----|------------|------------|------------|-------------|------------|------------|
| 1   | MLLSKFGSLA | HLCGPGGVDH | LPVKILQPAK | ADKESFEKVV  | QVGAVLGSGG | FGTVYAGSRI |
| 61  | ADGLPVAVKH | VVKERVTEWG | SLGGVAVPLE | VVLLRKVGAA  | GGARGVIRLL | DWFERPDGFL |
| 121 | LVLERPEPAQ | DLFDFITERG | ALDEPLARRF | FAQVLA AVRH | CHNCGVVHRD | IKDENLLVDL |
| 181 | RSSELKLIDF | GSGAVLKDTV | YTDFDGTRVY | SPPEWIRYHR  | YHGRSATVWS | LGVLLYDMVC |
| 241 | GDIPFEQDEE | ILRGRLFFRR | RVSPECQQLI | EWCLSLRPSE  | RPSLDQIAAH | PWMLGTEGSV |
| 301 | PENCDLRLCA | LDTDDGASTT | SSSESL     |             |            |            |

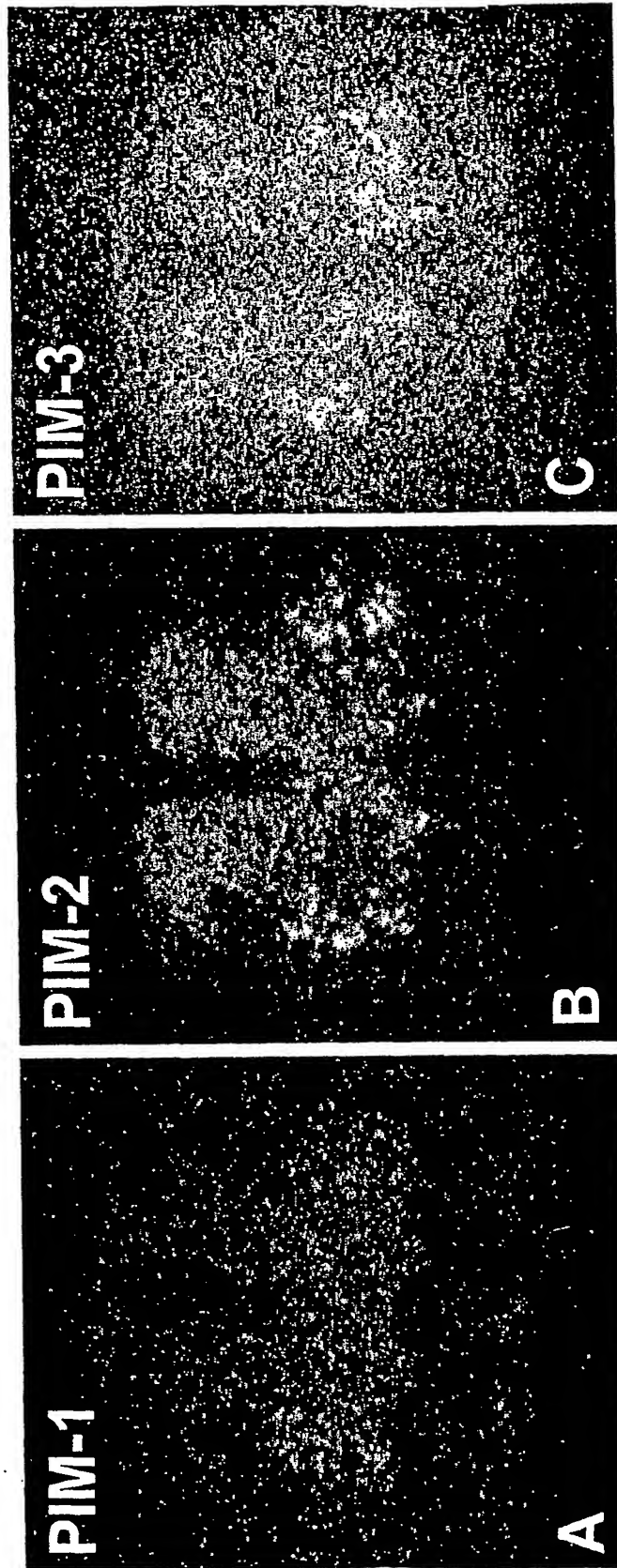


Fig. 3: mRNA Expression of PIM-kinases in the Lumbar Marrow of the Adult Rat

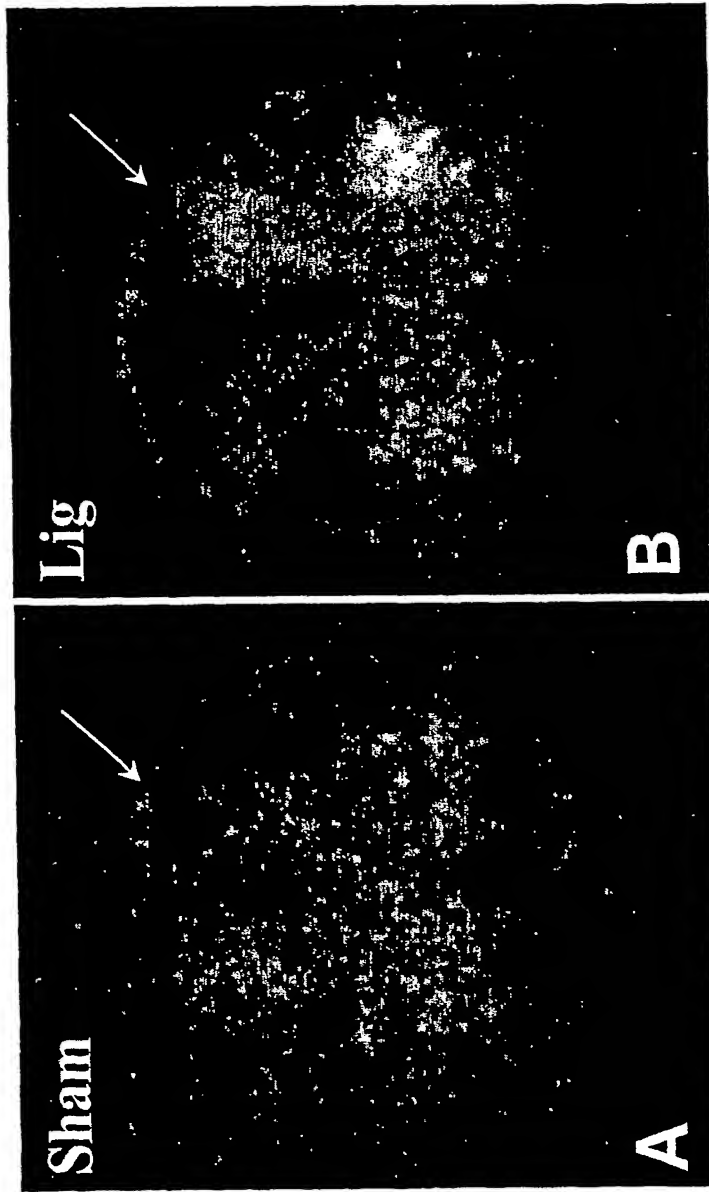
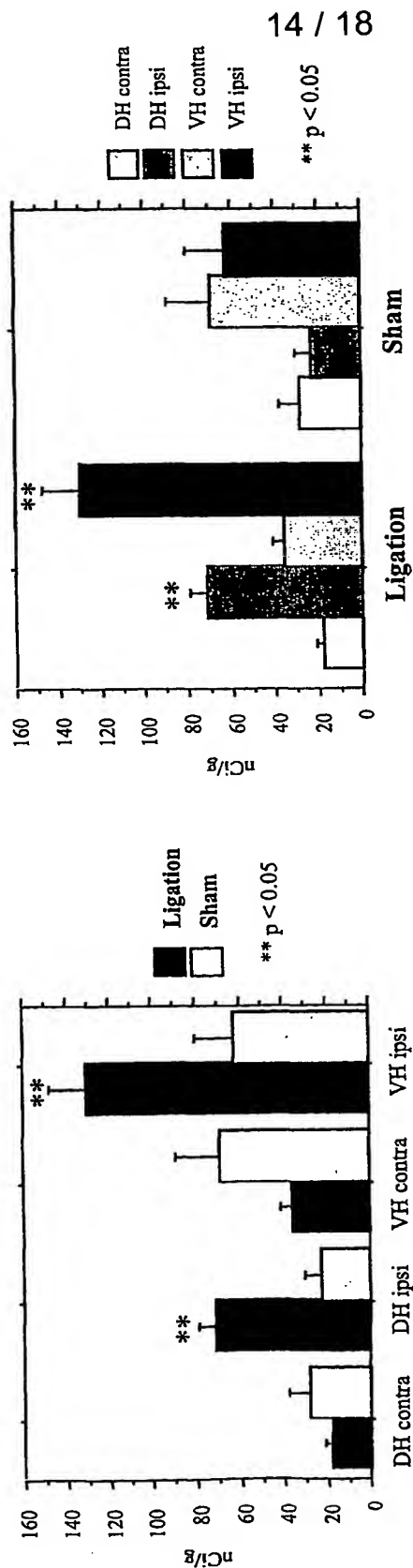


Fig 4: Changes in PIM-1 Gene Expression in the Spinal Cord (L5) after Ischiadicus Ligature (Bennett)

Fig. 5: PIM-1 mRNA Level in the Lumbar Marrow (L5) after Bennett Ligature  
 - Quantitative Evaluation of the *in situ* Hybridization Results -



| Group    | Region    | Measurements | Mean Value (nCi/g) | SD    | SEM   |
|----------|-----------|--------------|--------------------|-------|-------|
| Ligation | DH contra | 17           | 17,95              | 14,89 | 3,61  |
| Ligation | DH ipsi   | 17           | 71,61              | 30,05 | 7,29  |
| Ligation | VH contra | 17           | 35,19              | 22,37 | 5,43  |
| Ligation | VH ipsi   | 17           | 129,83             | 74,83 | 18,15 |
| Sham     | DH contra | 9            | 27,64              | 29,68 | 9,89  |
| Sham     | DH ipsi   | 9            | 21,94              | 24,52 | 8,17  |
| Sham     | VH contra | 9            | 69,30              | 57,77 | 19,26 |
| Sham     | VH ipsi   | 9            | 62,33              | 52,31 | 17,44 |

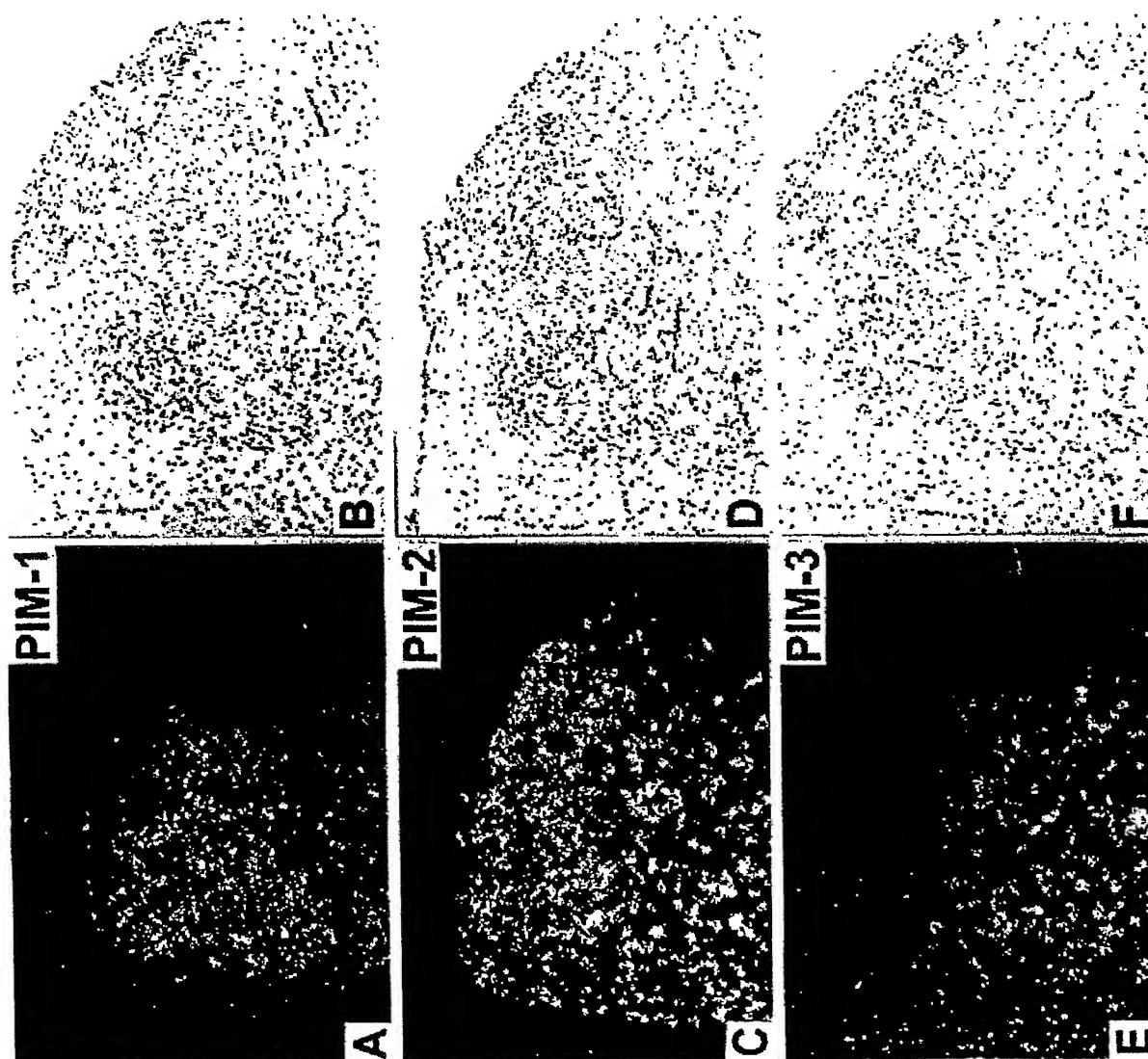


Fig. 6

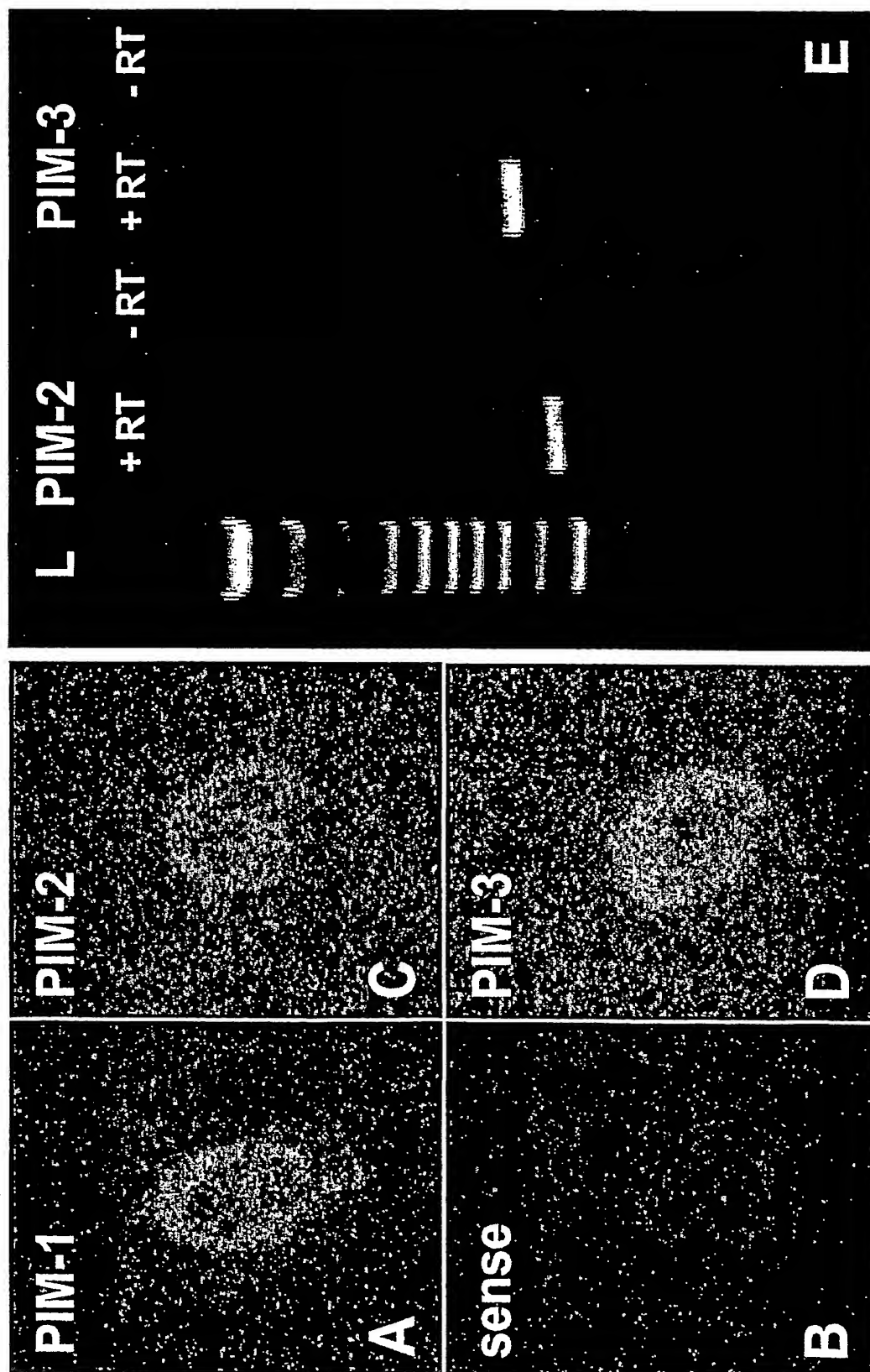


Fig. 7: mRNA Expression of PIM-kinases in the Spinal Ganglion



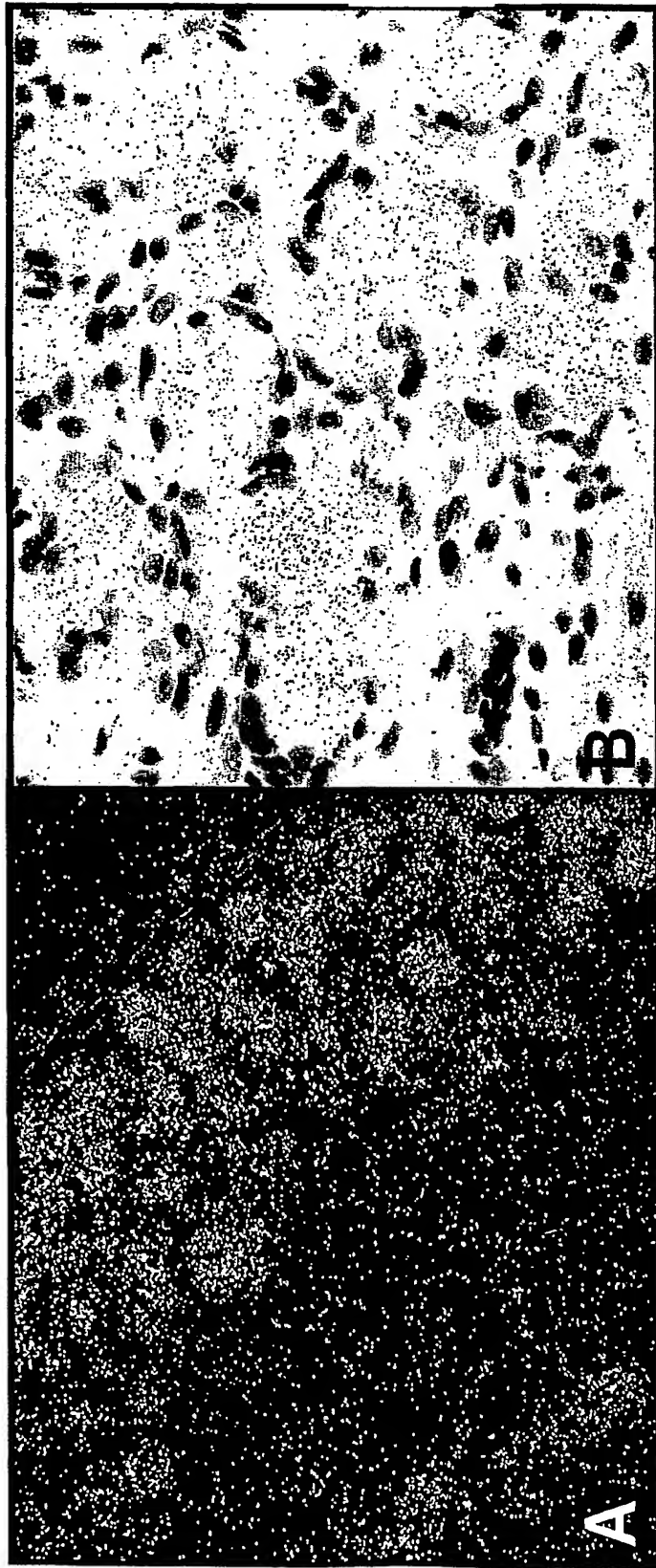


Fig. 8: Localization of PIM-1 Gene Expression in the Spinal Ganglion (L6) of the Rat with *in situ* Hybridization

Fig. 9: Changes in the PIM-1, PIM-2 and PIM-3 mRNA Level in the Spinal Ganglion L6 Following Bilateral CFA Arthritis  
- Semi-quantitative RT-PCR Analysis -

